Russel
09/807980

FILE 'REGISTRY' ENTERED AT 15:16:19 ON 15 JUL 2002
L1 8496 S GGFG/SQSP
L2 157 S L1 AND SQL=<8

FILE 'HCAPLUS' ENTERED AT 15:16:39 ON 15 JUL 2002
L3 75 S L2
L4 13 S L3 AND (DDS OR DRUG DELIVER? SYST?)
L5 9 S L3 AND ?ASSAY?
L6 20 S L4 OR L5

L6 ANSWER 1 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:185277 HCAPLUS
DOCUMENT NUMBER: 136:242899
TITLE: Phage display libraries and methods for identifying targeting peptides in humans in vivo
INVENTOR(S): Arap, Wadih; Pasqualini, Renata
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020723	A2	20020314	WO 2001-US28044	20010907

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-231266P P 20000908
US 2001-765101 A 20010117

AB The present invention concerns methods and compns. for identifying human targeting peptides sequences. The methods used for phage display biopanning in the mouse model system require substantial improvements for use with humans. In general, humans suitable for use with phage display are either brain dead or terminal wean patients. The amt. of phage library (preferably primary library) required for administration must be significantly increased, preferably 5 orders of magnitude to 1014 TU or higher, preferably administered i.v. in .apprx.200 mL of Ringer lactate soln. over about a 10-min period. To produce such large phage libraries, the transformed bacterial pellets recovered from up to 500-1000 transformations are amplified up to 10 times in the bacterial host, recovering the phage from each round of amplification and adding LB Tet medium to the bacterial pellet for collection of addnl. phage. Samples of various organs and tissues are collected starting .apprx.15 min after injection of the phage library; samples are processed and phage collected from each organ, tissue or cell type

of interest for DNA sequencing to det. the amino acid sequences of targeting peptides. A substantial improvement in the biopanning technique involves polyorgan targeting. It is possible to pool phage collected from multiple organs after a first round of biopanning and inject the pooled sample into a new subject, where each of the multiple organs may be collected for phage rescue, and the protocol repeated for as many rounds of biopanning as desired. In this manner, it is possible to significantly reduce the no. of subjects required for isolation of targeting peptides for multiple organs, while still achieving substantial enrichment of the organ-homing phage. Thus, 320 targeting peptides are identified with specificity for bone marrow, adipose tissue, skeletal muscle, prostate, skin, or multiple organs. The peptides are of use for targeted delivery of therapeutic agents, including gene therapy vectors. Such targeted delivery may be used for detection, diagnosis or treatment of human diseases. In certain embodiments, the peptide may be attached to an imaging agent and administered to a human to obtain an image or to diagnose a disease state. Also disclosed are a large no. of targeting peptide sequences and consensus motifs that are selective for human organs or tissues, obtained by the methods of the present invention.

IT **403702-00-1P**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeting peptide for human prostate; phage display libraries and methods for identifying targeting peptides in humans in vivo)

IT **403702-73-8P**
RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(targeting peptide for multiple organs; phage display libraries and methods for identifying targeting peptides in humans in vivo)

L6 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:148739 HCAPLUS
DOCUMENT NUMBER: 136:205403
TITLE: **DDS** compounds of drugs having hydroxy groups
INVENTOR(S): Ousu, Satoru; Oki, Hitoshi; Naito, Hiroyuki; Hirotani, Kenji
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002060351	A2	20020226	JP 2001-80188	20010321

PRIORITY APPLN. INFO.: JP 2000-79655 A 20000322
OTHER SOURCE(S): MARPAT 136:205403
AB The **DDS** (**drug delivery system**) compds. are represented by the formula AWN(R1)C(R2)(R3)OQ or

PZN(R1)C(R2)(R3)OQ [A = polymeric carrier for drugs; W = spacer contg. amino acid or oligopeptide residue linked to N at the C-terminal; P = protective group for H or NH2; Z = amino acid residue or oligopeptide residue linked to N at the C-terminal; R1-R3 = H, (substituted) alkyl, (substituted) aryl, carboxyl, alkoxycarbonyl; 2 of R1-R3 may form 4- to 8-membered ring; OQ = residue of OH-contg. drugs]. Tert-Bu 13-[[1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]-7-benzyl-2,5,8,11-tetraoxo-3,6,9,12-tetraazatri-1-decylcarbamate (prepn. given) showed 89% release of 1-[2-amino-6-[4-[(E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinol (I) in murine fibrosarcoma Meth-A cell homogenate at 40.degree. and pH 4.5 and <1% release of I in a buffer at pH 4.5. I.v. administration of a carboxymethyl dextran polyol deriv. of I (linked through an oligopeptide and aminomethylene linker) at 10 mg/kg as I showed significant antitumor effect and did not cause diarrhea in mice.

IT **401470-32-4P 401470-36-8DP**, conjugates with carboxymethyl dextran polyols
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for **DDS**)

IT **401470-35-7P 401470-36-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid or peptide derivs. of hydroxy-contg. drugs for **DDS**)

L6 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:71911 HCAPLUS
DOCUMENT NUMBER: 136:123681
TITLE: Pharmaceutical compositions containing **DDS** compounds
INVENTOR(S): Takahashi, Masayuki; Sugie, Shuichi; Takeuchi, Masahito
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002005855	A1	20020124	WO 2001-JP6020	20010711

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD,

TG
PRIORITY APPLN. INFO.: JP 2000-213083 A 20000713
AB Disclosed are pharmaceutical compns. which contain compds. obtained by bonding a carboxyl-bearing polysaccharide deriv. to a camptothecin deriv. either through a spacer or not there through and are improved in storage stability by the addn. of a sugar or a sugar alc. and, if necessary, a pH regulator. (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione conjugates with carboxymethyldextran using Gly-Gly-Phe-Gly spacer, are formulated with maltose and pH modifier to pH 6-9 to have a freeze-dried compn.
IT **200427-88-9D**, conjugates with camptothecin deriv. and carboxymethyldextran
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor compns. contg. camptothecin deriv. conjugates)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10548 HCAPLUS
DOCUMENT NUMBER: 136:74660
TITLE: **DDS** compounds containing drug-carboxymethyldextran polyalcohol conjugates and process for preparation thereof
INVENTOR(S): Imura, Akihiro; Noguchi, Shigeru; Yamaguchi, Tatsuya; Yagi, Tsutomu; Kawabe, Takefumi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000734	A1	20020103	WO 2001-JP5498	20010627
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067831	A5	20020108	AU 2001-67831	20010627

PRIORITY APPLN. INFO.: JP 2000-195919 A 20000629
JP 2000-2000195919A 20000629
WO 2001-JP5498 W 20010627

AB Disclosed is a **DDS** compd. which comprises (1S,9S)-1-amino-9-Et -5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]- pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13(9H,15H)-dione (I) as the drug compd. and carboxymethyldextran polyalc. and

in which the 1-position amino group of the former is bonded to the carboxyl groups of the latter through a spacer consisting of either one amino acid or 2 to 8 amino acids bonded by peptide linkages, characterized in that the amt. of the drug compd. residue introduced is 3.2-8.4 % and that the carboxymethyldextran polyalc. has an av. mol. wt. of 240,000-480,000 and a degree of carboxymethylation of 0.14-0.47. Also disclosed is a process for the prepn. of the **DDS** compd. which comprises the step of adding an aq. soln. of sodium periodate to an aq. soln. of dextran at a temp. of 4.degree. .+-. 2.degree. to oxidize the dextran, and then adding the resulting reaction fluid to an aq. soln. of sodium borohydride at a temp. of .ltoreq. 15.degree. to thereby obtain dextran polyalc. A conjugate of I and carboxymethyldextran polyalc. with tetrapeptide spacer Gly-Gly-Phe-Gly was prepd., and its antitumor effect in Meth A cell-bearing mice was examd.

IT **384828-78-8DP**, reaction products with carboxymethyldextran polyalc.
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antitumor drug-carboxymethyldextran polyalc. conjugates with peptide spacers)

IT **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antitumor drug-carboxymethyldextran polyalc. conjugates with peptide spacers)

IT **223537-08-4P 384828-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antitumor drug-carboxymethyldextran polyalc. conjugates with peptide spacers)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:611691 HCAPLUS
DOCUMENT NUMBER: 135:191315
TITLE: Polynucleotides and polypeptides for Candida RHO1, CDC42, and RAM2 genes, and their uses related to identifying antifungal agents
INVENTOR(S): Berlin, Vivian; Damagnez, Veronique; Smith, Susan E.
PATENT ASSIGNEE(S): GPC Biotech Inc., USA
SOURCE: U.S., 70 pp., Cont.-in-part of U.S. Ser. No. 771,212.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6277564	B1	20010821	US 1997-838973	19970423
US 6117641	A	20000912	US 1996-631319	19960411
CA 2251593	AA	19971016	CA 1997-2251593	19970411
KR 2000005397	A	20000125	KR 1998-8128	19981012

PRIORITY APPLN. INFO.: US 1996-631319 A2 19960411
US 1996-771212 A2 19961220

AB This invention claims novel Candida polynucleotides and gene products, their recombinant expression and prodn., and isolation of recombinant polypeptides. The polynucleotides identify Candida albicans genes RHO1, CDC42, and RAM2. Candida genes RHO1 and CDC42, named according to their sequence homol. to Saccharomyces cerevisiae genes, encode G proteins (also called GTPases) involved in signal transduction pathways regulating yeast protein kinase C homologs and glucan synthase and involved in cell wall integrity. Gene RAM2 encodes the shared .alpha. subunit of farnesyl-protein transferase (FPTase) and geranylgeranyl protein transferase I (GGPTase I). Genetic interactions and biochem. evidence from budding yeast suggest that Rho1p and Cdc42p GTPases are substrates of GGPTase and that prenylation of G proteins may affect their assocn. with protein kinase C and glucan synthase activity. The present invention may be used in **assays** for screening and identifying pharmaceutically effective compds. that specifically inhibit the biol. activity of fungal GTPase proteins, particularly GTPases involved in cell wall integrity, hyphal formation, and/or other cellular functions crit. to pathogenesis.

IT **87742-82-3**
RL: PRP (Properties)
(unclaimed sequence; polynucleotides and polypeptides for Candida RHO1, CDC42, and RAM2 genes, and their uses related to identifying antifungal agents)

REFERENCE COUNT: 96 THERE ARE 96 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:578088 HCAPLUS
DOCUMENT NUMBER: 135:162483
TITLE: **Assays** and reagents for identifying antifungal agents, and related uses
INVENTOR(S): Berlin, Vivian; Levin, David E.; Ohya, Yoshikazu; Damagnez, Veronique; Smith, Susan E.
PATENT ASSIGNEE(S): GPC-Biotech Inc., USA; The Johns Hopkins University
SOURCE: U.S., 72 pp., Cont.-in-part of U.S. Ser. No. 771,212.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6271197	B1	20010807	US 1997-842306	19970423
US 6117641	A	20000912	US 1996-631319	19960411
CA 2251593	AA	19971016	CA 1997-2251593	19970411
KR 2000005397	A	20000125	KR 1998-8128	19981012

PRIORITY APPLN. INFO.: US 1996-631319 A2 19960411
US 1996-771212 A2 19961220

AB The invention provides rapid, reliable, and effective **assays** for screening and identifying pharmaceutically effective compds. that specifically inhibit the biol. activity of fungal GTPase

proteins, particularly GTPases involved in cell wall integrity, hyphael formation, and/or other cellular functions crit. to pathogenesis. Another aspect of the present invention relates to novel Candida genes and gene products.

IT **87742-82-3**
RL: PRP (Properties)
(unclaimed sequence; **assays** and reagents for identifying antifungal agents, and related uses)

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:322648 HCAPLUS
DOCUMENT NUMBER: 135:185307
TITLE: Characteristics of tissue distribution of various polysaccharides as drug carriers: influences of molecular weight and anionic charge on tumor targeting
AUTHOR(S): Sugahara, Shuichi; Okuno, Satoshi; Yano, Toshiro; Hamana, Hiroshi; Inoue, Kazuhiro
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2001), 24(5), 535-543
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Using the Walker 256 model for carcinosarcoma-bearing rats, we i.v. administered 5 polysaccharide carriers with various mol. wts. (MWs) and elec. charges and tested for their plasma and tissue distribution. Two carriers, carboxymethylated-D-manno-D-glucan (CMMG) and CMdextran (CMDex), showed higher plasma AUC than the other carriers tested, namely, CMchitin (CMCh), N-desulfated N-acetylated heparin (DSH), and hyaluronic acid (HA). This was consistently found to be true over the range of MWs tested. For CMDex, the max. value of plasma AUC was obtained when the MW exceeded 150 kDa. As for the anionic charge, CMDex (110-180 kDa) with a degree of substitution (DS) of the CM groups ranging from 0.2 to 0.6, showed max. plasma AUC values. Twenty-four hours after administration, the concn. of CMDex (180-250 kDa; DS: 0.6-1.2) in tumors was more than 3% of dose/g-approx. 10-fold higher than those obsd. with CMCh, DSH and HA. Doxorubicin (DXR) was bound to these carriers via a peptide spacer, GlyGlyPheGly (GGFG), to give carrier-GGFG-DXR conjugates (DXR content: 4.2-7.0 (wt./wt.)%), and the antitumor effects of these conjugates were tested with Walker 256 carcinosarcoma-bearing rats by monitoring the tumor wts. after a single i.v. injection. Compared with free DXR, CMDex-GGFG-DXR and CMMG-GGFG-DXR conjugates significantly suppressed tumor growth, while the CMCh-GGFG-DXR, DSH-GGFG-DXR, and HA-GGFG-DXR conjugates in a similar comparison showed weak tumor growth inhibition. These findings suggest that the antitumor effect of the carrier-DXR conjugates was related to the extent with which the carriers accumulated in the tumors.

IT **200427-88-9DP**, conjugates with doxorubicin and polysaccharides
RL: BAC (Biological activity or effector, except adverse); BPR

(Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effects of mol. wt. and anionic charge of polysaccharide drug carriers on tumor targeting)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:832857 HCAPLUS
DOCUMENT NUMBER: 134:256691
TITLE: Determinants for the drug release from T-0128, camptothecin analog-carboxymethyl dextran conjugate
AUTHOR(S): Harada, M.; Sakakibara, H.; Yano, T.; Suzuki, T.; Okuno, S.
CORPORATE SOURCE: Discovery Research Laboratory, Tanabe Seiyaku Co. Ltd., Yodogawa-ku, Osaka, 532-8505, Japan
SOURCE: Journal of Controlled Release (2000), 69(3), 399-412
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To improve pharmacol. profiles of camptothecins (CPTs), a new macromol. prodrug, denoted T-0128, was synthesized. This prodrug comprises a novel CPT analog (T-2513: 7-ethyl-10-aminopropyloxy-CPT) bound to carboxymethyl (CM) dextran through a Gly-Gly-Gly linker, with a mol. wt. of 130 kDa. The present study was designed to elucidate the mechanisms that promote the release of linked T-2513. First, we compared the abilities of a rat liver homogenate, a cocktail of its lysosomal enzymes, and different types of pure enzymes, to liberate T-2513 from the conjugate. The releasing rate in the homogenate was very slow, but was accelerated with the lysosomes. Lysosomal cysteine proteinases, such as cathepsin B, were responsible, coupled with the results of in vitro and in vivo inhibition studies using proteinase inhibitors. The pH optimum for the cathepsin B-mediated drug release was approx. 4. This corresponds to the pH in lysosomes, suggesting lysosomotropic release. Second, to assess the effect of the length and compn. of the peptidyl linker, we synthesized the conjugates with a different linker and compared the drug-releasing rates. We found that the insertion of Phe into Gly-Gly-Gly allowed various kinds of enzymes to produce a rapid cleavage, and the Gly-chain lengthening enhanced the lysosome-mediated drug release. The released T-2513 levels in the liver and tumor of the tumor-bearing rats dosed with each conjugate increased with the length of Gly linker, suggesting a good in vitro to in vivo relationship. Comparative efficacy studies of the conjugates with a different linker demonstrated that T-0128 showed the max. efficacy against MX-1 human mammary xenograft tumors. Thus the Gly-Gly-Gly linker exploits lysosomal cathepsin B to release T-2513 slowly and steadily, resulting in improved therapeutic efficacy.

IT **193097-95-9P**
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(determinants for drug release from T-0128 camptothecin

analog-carboxymethyl dextran conjugate)
IT **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran conjugate)
IT **192991-32-5P 192991-33-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(determinants for drug release from T-0128 camptothecin analog-carboxymethyl dextran conjugate)
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:314580 HCAPLUS
DOCUMENT NUMBER: 132:326152
TITLE: **DDS** compounds and method for **assaying** the same
INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi; Ikeda, Masahiro; Shiose, Yoshinobu; Korenaga, Hiroshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000025825	A1	20000511	WO 1999-JP6016	19991029
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964880	A1	20000522	AU 1999-64880	19991029
BR 9915198	A	20010814	BR 1999-15198	19991029
EP 1155702	A1	20011121	EP 1999-952805	19991029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001002128	A	20010620	NO 2001-2128	20010430

PRIORITY APPLN. INFO.:
JP 1998-310130 A 19981030
JP 1998-329272 A 19981119
WO 1999-JP6016 W 19991029

AB The invention relates to a method for **assaying** a **DDS** compd. contg. a saccharide compd.-modified carboxy C1-4 alkyldextran polyalc. and a drug compd. [DX8951 or doxorubicin] residue bonded to this carboxy C1-4 alkyldextran polyalc., or a **DDS** compd. wherein a polymer carrier is bonded to a drug compd. residue via a spacer contg. 2 to 8 amino acids bonded together via peptide bonds, which involves the step of

assaying a hydrolyzate obtained by treating the **DDS** compd. with peptidase.

IT **200427-88-9DP**, DX8951 or doxorubicin conjugates with carboxy C1-4 alkyldextran polyalc. and
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**DDS** compds. and method for **assaying** the same)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:311210 HCAPLUS
DOCUMENT NUMBER: 133:155250
TITLE: Distribution characteristics of carboxymethyl pullulan-peptide-doxorubicin conjugates in tumor-bearing rats: different sequence of peptide spacers and doxorubicin contents
AUTHOR(S): Nogusa, Hideo; Yamamoto, Keiji; Yano, Toshiro; Kajiki, Masahiro; Hamana, Hiroshi; Okuno, Satoshi
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2000), 23(5), 621-626
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasma and tissue distribution of conjugates of CM-pullulan (CMPul) and doxorubicin (DXR), either bound directly or through three types of tetrapeptide spacers, was studied after i.v. injection to rats bearing Walker 256 carcinosarcoma and compared with that of DXR. In contrast to DXR, each conjugate retained high levels of DXR in the conjugated form in plasma and displayed high accumulation in the tumor at 6 h after the administration. Disposition characteristics of [3H]CMPul in rats bearing Walker 256 carcinosarcoma indicate that pullulan, which had mol. wt. over 50 kDa, is a suitable macromol. carrier for tumor targeting in cancer chemotherapy by carboxymethylation. We find that the in vivo antitumor effect of the conjugates depends on the tumor AUC of free DXR released from the conjugates. CMPul-DXR conjugates were also distributed in the reticuloendothelial organs, such as liver, spleen and bone marrow; however, the tissue concns. of the conjugates in the heart, lung and muscle were lower than those of DXR. We next investigated the effect of the DXR contents of CMPul-DXR conjugates on their body distribution in rats bearing Walker 256. The half life of CMPul-DXR conjugates in plasma were shorter and the conjugates had greater accumulation in the reticuloendothelial system, while they showed lower concns. in the tumor with increasing DXR contents. Antitumor activity of CMPul-DXR conjugates were reduced and the lethal toxicities of CMPul-DXR conjugates were amplified with increasing DXR contents.

IT **161254-06-4D**, reaction products with sodium carboxymethylpullulan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU

(Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(peptide spacers and doxorubicin contents effect on pharmacokinetics and antitumor activity of CM-pullulan-peptide-doxorubicin conjugates in tumor-bearing rats)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:146878 HCAPLUS
DOCUMENT NUMBER: 132:288308
TITLE: Structure-activity relationships of carboxymethylpullulan-peptide-doxorubicin conjugates: Systematic modification of peptide spacers
AUTHOR(S): Nogusa, Hideo; Yano, Toshiro; Kashima, Nobukazu; Yamamoto, Keiji; Okuno, Satoshi; Hamana, Hiroshi
CORPORATE SOURCE: Drug Delivery System Institute, Ltd., Chiba, 278-0022, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(3), 227-230
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of carboxymethylpullulan (CMPul)-doxorubicin (DXR) conjugates bound by peptide spacers of different compns. and lengths were prepd. and evaluated for their in vivo antitumor effects. Systematic study of the peptide spacers indicated that CMPul-DXR conjugates bound via appropriate dipeptide spacers were more potent than DXR.
IT **264192-71-4D**, conjugates with CM-pullulan
264192-72-5D, conjugates with CM-pullulan
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(structure-antitumor activity relationships of CM-pullulan-peptide-doxorubicin conjugates)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:763905 HCAPLUS
DOCUMENT NUMBER: 132:15631
TITLE: Antitumor or antiinflammatory drug composites
INVENTOR(S): Susaki, Hiroshi; Inoue, Kazuhiro; Kuga, Hiroshi
PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9961061	A1	19991202	WO 1999-JP2681	19990521
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937333	A1	19991213	AU 1999-37333	19990521
EP 1080732	A1	20010307	EP 1999-919664	19990521
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
NO 2000005913	A	20010122	NO 2000-5913	20001122
PRIORITY APPLN. INFO.:			JP 1998-140915 A	19980522
			WO 1999-JP2681 W	19990521

AB Drug composites useful as **DDS** compds., which are represented by the general formula: A-R-NH-Y-CH2-O-CO-Q (wherein A is a polymer serving as a carrier for a drug; R is a spacer comprising one amino acid mol. or one comprising 2 to 8 amino acid mols. bound to each other through peptide linkage; Y is optionally substituted phenylene; and Q is a residue of a drug compd. such as an antitumor agent). The composites permit the speedy and regioselective release of drug compds. such as antitumor or anti-inflammatory agents, thus exhibiting expected drug effects without fail. A composite of DX-8951 [(1S,9S)-1-Amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-10,13(9H,15H)-dione] was prepd. from DX-8951 methanesulfonic acid salt, dextran polyalc. Na salt, Boc-Gly-Gly-Phe-Gly-OH, 4-aminobenzylalc., and bis(4-nitrophenyl)carbonate.

IT **251459-33-3DP**, reaction products with dextran and acetic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of antitumor or antiinflammatory drug dextran polyalc. conjugates)

IT **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antitumor or antiinflammatory drug dextran polyalc. conjugates)

IT **251459-28-6P 251459-29-7P 251459-31-1P 251459-32-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antitumor or antiinflammatory drug dextran polyalc. conjugates)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:224542 HCAPLUS
DOCUMENT NUMBER: 130:316621
TITLE: Drug conjugates comprising carboxyalkyl pullulan

polyalcohol carriers bonded with pharmaceutically active agents through peptide spacers
INVENTOR(S): Inoue, Kazuhiro; Suzaki, Hiroshi; Ikeda, Masahiro
PATENT ASSIGNEE(S): Daiichi Seiyaku Co., Ltd., Japan; Dds Kenkyusho K. K.
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11092405	A2	19990406	JP 1997-254780	19970919

AB The invention provides a drug conjugate suitable for an improved **drug delivery system** of an antitumor agent or an anti-inflammatory agent, wherein the conjugate contains a carboxy C1-4 alkyl pullulan polyalc. carrier bonded with a pharmaceutically active agent residue through a spacer consisting of an amino acid or a peptide with 2-8 amino acids. An antitumor conjugate consisting of carboxymethyl pullulan polyalc.-Gly-Gly-Phe-Gly-(DX-8951) was prepd. The conjugate exhibited higher antitumor effect with lower injection doses in Meth A-bearing mice as compared with the effect of unconjugated DX-8951.

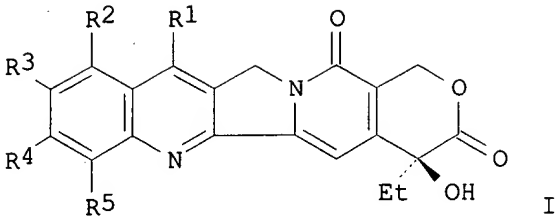
IT **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of drug conjugates comprising carboxyalkyl pullulan polyalc. carriers bonded with drugs through peptide spacers)

IT **223537-08-4P 223537-11-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of drug conjugates comprising carboxyalkyl pullulan polyalc. carriers bonded with drugs through peptide spacers)

L6 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:183845 HCAPLUS
DOCUMENT NUMBER: 130:287052
TITLE: Anticancer drug compositions for targeting therapy
INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Tetsu; Yano, Toshiaki
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11071280	A2	19990316	JP 1998-175240	19980623

PRIORITY APPLN. INFO.: JP 1997-169746 19970626
OTHER SOURCE(S): MARPAT 130:287052
GI



I

AB Anticancer drug compns. for targeting therapy are prepd. by conjugating camptothecin derivs. (I) [R1-5 : e.g. 2 adjacent groups may be H or may form alkylene linkage, 1 group is XnAlkmR6 and the other 2 groups are H (R6 = NH2, OH, etc. ; X = O or NH; Alk = alkylene; m and n = 0 or 1)] with polysaccharides via amino acids or peptides. The compns. are useful for treating lung cancer, ovary cancer, uterus cancer, mammary cancer, digestive tract cancer, lung cancer, kidney cancer, prostate cancer, neck cancer, malignant lymphoma and leukemia.

IT **187794-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of anticancer drug compns. for targeting therapy)

IT **192990-96-8P 192991-18-7P 192991-20-1P 192991-22-3P 192991-23-4P 192991-24-5P 192991-25-6P 192991-32-5P 192991-33-6P 192991-34-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of anticancer drug compns. for targeting therapy)

IT **192990-91-3DP**, reaction product with sodium carboxymethyl dextran **192990-93-5DP**, reaction product with sodium carboxymethyl dextran **192990-94-6DP**, reaction product with sodium carboxymethyl dextran **192990-95-7DP**, reaction product with sodium carboxymethyll dextran **192990-96-8DP**, reaction product with sodium carboxymethyl dextran
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of anticancer drug compns. for targeting therapy)

L6 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:760819 HCAPLUS
DOCUMENT NUMBER: 130:106811
TITLE: Evaluation of resins for on-bead screening: a study of papain and chymotrypsin specificity using PEGA-bound combinatorial peptide libraries
AUTHOR(S): Leon, Susanna; Quarrell, Rachel; Lowe, Gordon
CORPORATE SOURCE: Dyson Perrins Laboratory, Oxford University, Oxford, OX1 3QY, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(21), 2997-3002
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB TentaGel, ArgoGel and PEGA resins were evaluated for on-bead biol.

screening, using a fluorescently-labeled peptide attached to each and **assayed** for papain activity. Peptide attached to PEGA was cleaved in near quant. yield at the expected sites, while an identical sequence on TentaGel and ArgoGel beads was hydrolyzed in very low yields and nonspecifically on ArgoGel. The compatibility of PEGA with enzymes was further demonstrated by the detn. of subsite specificities of papain and chymotrypsin using PEGA-bound peptide libraries, which proved to be similar to those obsd. in free soln.

IT **219657-42-8D**, resin bound
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)
(study of papain and chymotrypsin specificity using PEGA-bound combinatorial peptide libraries)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:336502 HCAPLUS
DOCUMENT NUMBER: 125:2993
TITLE: Cloning and expression of Bacillus thuringiensis morrisoni cryIF delta-endotoxin gene and control of lepidopteran pests
INVENTOR(S): Payne, Jewel; Sick, August J.; Narva, Kenneth E.; Schnepf, H. Ernest; Schwab, George E.
PATENT ASSIGNEE(S): Mycogen Corporation, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9605314	A2	19960222	WO 1995-US10310	19950814
WO 9605314	A3	19960328		
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5686069	A	19971111	US 1994-291368	19940815
AU 9533247	A1	19960307	AU 1995-33247	19950814
AU 711479	B2	19991014		
EP 776368	A2	19970604	EP 1995-929514	19950814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504196	T2	19980428	JP 1995-507560	19950814

PRIORITY APPLN. INFO.:
US 1994-291368 19940815
US 1990-597607 19901015
US 1993-32778 19930306
WO 1995-US10310 19950814

AB Disclosed and claimed are novel Bacillus thuringiensis isolates which have lepidopteran activity. Thus, these isolates, or mutants thereof, can be used to control such insect pests. Further, genes encoding novel .delta.-endotoxins can be removed form the isolates and transferred to other host microbes, or plants. Expression of

the .delta.-endotoxins in such hosts results in the control of susceptible insect pests in the environment of such hosts. Eighteen different B. thuringiensis isolates were cultured and **assayed** for activity against Trichoplusia ni and Spodoptera exigua. Addnl., the toxin genes of these isolates were characterized by RFLP anal. The cryIF(a) gene of B. thuringiensis morrisoni strain PS91C2 was cloned, sequenced, and expressed in Escherichia coli and cry- B. thuringiensis. The recombinant toxin had an LC50 against Plutella xylostella of 5 .mu.g/mL diet.

IT **177261-43-7**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(oligonucleotide encoding; cloning and expression of Bacillus thuringiensis morrisoni cryIF delta-endotoxin gene and control of lepidopteran pests)

L6 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:676982 HCAPLUS
DOCUMENT NUMBER: 123:286659
TITLE: Liquid-phase combinatorial synthesis
AUTHOR(S): Han, Hyunsoo; Wolfe, Mary M.; Brenner, Sydney; Janda, Kim D.
CORPORATE SOURCE: Dep. Mol. Biol. Chem., Scripps Res. Inst., La Jolla, CA, 92037, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(14), 6419-23
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A concept termed liq.-phase combinatorial synthesis (LPCS) is described. The central feature of this methodol. is that it combines the advantages that classic org. synthesis in soln. offers with those that solid-phase synthesis can provide, through the application of a linear homogeneous polymer. To validate this concept two libraries were prepd., one of peptide and the second of nonpeptide origin. The peptide-based library was synthesized by a recursive deconvolution strategy (E. Erb, et al., 1994), and several ligands found in this library bind a monoclonal antibody elicited against .beta.-endorphin. The non-peptide mols. were arylsulfonamides, a class of compds. of known clin. bactericidal efficacy. The results indicate that the reaction scope of LPCS should be general, and its value to multiple, high-throughput screening **assays** could be of particular merit, since multi-milligram quantities of each library member can readily be attained.

IT **169692-79-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(liq.-phase combinatorial synthesis of peptides and arylsulfonamides)

L6 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:123965 HCAPLUS
DOCUMENT NUMBER: 120:123965
TITLE: Discovery of biologically active peptides in random libraries: solution-phase testing after staged orthogonal release from resin beads
AUTHOR(S): Salmon, Sydney E.; Lam, Kit S.; Lebl, Michal;

Kandola, Anitha; Khattri, Parth S.; Wade, Shelly; Patek, Marcel; Kocis, Petr; Krchnak, Viktor; et al.
CORPORATE SOURCE: Coll. Med., Univ. Arizona, Tucson, AZ, 85724, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1993), 90(24), 11708-12
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To speed drug discovery, the authors developed an approach for identification of individual peptides with a desired biol. activity from a library contg. millions of peptides. The approach uses sequential orthogonal release of chem. synthesized peptides from insol. beads, followed by testing in soln. In this system, each bead within a library of beads has one peptide sequence, but peptide mols. are attached to the bead with three types of chem. linkers, including two linkers cleavable at different pH optima. An uncleavable linker keeps some peptide attached to the bead for sequencing positives from the soln. **assay**. Applicability of this discovery technique was documented by identifying ligands for a monoclonal antibody and for the human platelet fibrinogen receptor, glycoprotein IIb/IIIa.
IT **153012-44-3**
RL: ANST (Analytical study)
(.beta.-endorphin monoclonal antibodies binding by, method for discovery of)

L6 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:567122 HCAPLUS
DOCUMENT NUMBER: 117:167122
TITLE: Selective enrichment and characterization of high affinity ligands from collections of random peptides on filamentous phage
AUTHOR(S): Barrett, Ronald W.; Cwirla, Steven E.; Ackerman, Martha S.; Olson, Ann M.; Peters, Elizabeth A.; Dower, William J.
CORPORATE SOURCE: Dep. Mol. Pharmacol., Affymax Res. Inst., Palo Alto, CA, 94304, USA
SOURCE: Anal. Biochem. (1992), 204(2), 357-64
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Large collections of random peptides can be expressed on the N-terminus of the pIII protein of filamentous phage and screened for binding to antibodies and other receptors. In the previous work with a monoclonal antibody (3E7) (1990), it was shown that a high proportion of the selected peptides had relative low affinity (Kd's > 1 .mu.M). Conditions for selective enrichment of phage expressing high affinity peptides are described. This is done by allowing the phage to interact with a low concn. of 3E7 Fab followed by extensive washing to allow dissocn. of phage-bearing peptides with low affinity. These affinity selection conditions were applied to the pool of phage previously selected using a high concn. of IgG. A phage clone with the known high affinity ligand YGGFL (Kd 7.1 nM) and several other closely related peptides were isolated. The dissocn. rate of 125I-3E7 Fab from several phage clones approximated that of phage expressing YGGFL. A good correlation was found

between the dissocn. rate of the peptides found on phage and the equil. binding consts. of chem. synthesized peptides. The strategy of using a low concn. of receptor and extensive washing to select phage-bearing high affinity peptides, combined with **assays** to det. the specificity and relative affinity of peptides on isolated phage clones, should be generally applicable in using the peptides-on-phage system for discovery of high affinity receptor ligands.

IT **143740-83-4**
RL: ANST (Analytical study)
(monoclonal antibody dissocn. from phages bearing)

L6 ANSWER 20 OF 20 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:16289 HCAPLUS
DOCUMENT NUMBER: 88:16289
TITLE: Structural requirements for opioid activity of analogs of the enkephalins
AUTHOR(S): Beddell, C. R.; Clark, R. B.; Hardy, G. W.; Lowe, L. A.; Ubatuba, F. B.; Vane, J. R.; Wilkinson, S.; Chang, K. J.; Cuatrecasas, P.; Miller, R. J.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, Engl.
SOURCE: Proc. R. Soc. London, Ser. B (1977), 198(1132), 249-65
CODEN: PRLBA4
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Structure-activity relations of a series of analogs of the 2 endogenous morphine-like peptides, leucine-enkephalin [58822-25-6] and methionine-enkephalin [58569-55-4] were examd. on the basis of effects on the mouse vas deferens and the guinea pig ileum and affinities for the rat brain opiate receptor. In the mouse vas deferens, metab. of the peptides by proteolysis was not a major influence on activity. In contrast, however, brain opiate receptor prepns. contained an abundance of proteolytic enzymes, the effects of which were minimized by conducting opiate receptor binding **assays** at 0.degree. and in the presence of bacitracin. The potentiation of biol. activity ad opiate receptor binding affinity by replacing the Gly2 residue in the natural enkephalins by D-Ala, is discussed both in terms of increased stability of the Tyr-D-Ala bond to aminopeptidases and of the stabilization of the peptide conformation as present in the receptor-peptide complex. The substitution of the Leu5- or Met5-residue by the corresponding D-amino acid contributed little to proteolytic stability, which emphasizes that the predominating site at which metab. occurs is the Tyr1-Gly2 bond. Of the analogs described, [D-Ala2,D-Leu5]-enkephalin [63631-40-3] was the most active peptide in the 3 **assay** systems. Substitutions by the resp. D-amino acids D-Tyr and D-Phe at positions 1 and 4 decreased both the potency and binding affinity and emphasized the importance of stereochem. acceptability at these positions.

IT **61064-76-4**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(opioid activity of)

E1 THROUGH E40 ASSIGNED

FILE 'REGISTRY' ENTERED AT 15:17:27 ON 15 JUL 2002
L7 40 SEA FILE=REGISTRY ABB=ON PLU=ON (187794-49-6/BI OR
200427-88-9/BI OR 192990-96-8/BI OR 192991-32-5/BI OR
192991-33-6/BI OR 223537-08-4/BI OR 384828-78-8/BI OR
401470-36-8/BI OR 87742-82-3/BI OR 143740-83-4/BI OR
153012-44-3/BI OR 161254-06-4/BI OR 169692-79-9/BI OR
177261-43-7/BI OR 192990-91-3/BI OR 192990-93-5/BI OR
192990-94-6/BI OR 192990-95-7/BI OR 192991-18-7/BI OR
192991-20-1/BI OR 192991-22-3/BI OR 192991-23-4/BI OR
192991-24-5/BI OR 192991-25-6/BI OR 192991-34-7/BI OR
193097-95-9/BI OR 219657-42-8/BI OR 223537-11-9/BI OR
251459-28-6/BI OR 251459-29-7/BI OR 251459-31-1/BI OR
251459-32-2/BI OR 251459-33-3/BI OR 264192-71-4/BI OR
264192-72-5/BI OR 401470-32-4/BI OR 401470-35-7/BI OR
403702-00-1/BI OR 403702-73-8/BI OR 61064-76-4/BI)

L8 40 L7 AND L2

L8 ANSWER 1 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **403702-73-8** REGISTRY
CN L-Arginine, L-arginylglycylglycyl-L-phenylalanylglycyl-L-valyl-
(9CI) (CA INDEX NAME)
SQL **7**

SEQ 1 RGGFGVR
====
HITS AT: 2-5

REFERENCE 1: 136:242899

L8 ANSWER 2 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **403702-00-1** REGISTRY
CN L-Glutamine, L-alanylglycylglycyl-L-phenylalanylglycyl-L-.alpha.-
glutamyl- (9CI) (CA INDEX NAME)
SQL **7**

SEQ 1 AGGFGEQ
====
HITS AT: 2-5

REFERENCE 1: 136:242899

L8 ANSWER 3 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **401470-36-8** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-
3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-
pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA
INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:205403

L8 ANSWER 4 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **401470-35-7** REGISTRY

CN Glycinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:205403

L8 ANSWER 5 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **401470-32-4** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[[1-[2-amino-6-[4-[(1E)-3-[4-(3,5-difluorophenyl)-1-piperazinyl]-1-propenyl]-5-methyl-1H-pyrazol-1-yl]-4-pyrimidinyl]-3-azetidinyl]oxy]methyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:205403

L8 ANSWER 6 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **384828-78-8** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:74660

L8 ANSWER 7 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **264192-72-5** REGISTRY
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[(glycylglycyl-L-phenylalanylglycyl)amino]-.alpha.-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 132:288308

L8 ANSWER 8 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **264192-71-4** REGISTRY
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[(glycylglycylglycyl-L-phenylalanylglycyl)amino]-.alpha.-L-lyxo-hexopyranosyl]oxy]-, (8S,10S)- (9CI) (CA INDEX NAME)
SQL **5**

SEQ 1 GGGFG
====
HITS AT: 2-5

REFERENCE 1: 132:288308

L8 ANSWER 9 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **251459-33-3** REGISTRY
CN Glycinamide, N-acetylglycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 132:15631

L8 ANSWER 10 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **251459-32-2** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 132:15631

L8 ANSWER 11 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **251459-31-1** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[4-[[[[[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]amino]carbonyl]oxy]methyl]phenyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG

```
            ====
HITS AT:    1-4

REFERENCE   1:  132:15631

L8   ANSWER 12 OF 40  REGISTRY  COPYRIGHT 2002 ACS
RN   251459-29-7  REGISTRY
CN   Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-
     phenylalanyl-N-[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenyl]-
     (9CI)  (CA INDEX NAME)
SQL  4

SEQ      1 GGFG
            ====
HITS AT:    1-4

REFERENCE   1:  132:15631

L8   ANSWER 13 OF 40  REGISTRY  COPYRIGHT 2002 ACS
RN   251459-28-6  REGISTRY
CN   Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-
     phenylalanyl-N-[4-(hydroxymethyl)phenyl]- (9CI)  (CA INDEX NAME)
SQL  4

SEQ      1 GGFG
            ====
HITS AT:    1-4

REFERENCE   1:  132:15631

L8   ANSWER 14 OF 40  REGISTRY  COPYRIGHT 2002 ACS
RN   223537-11-9  REGISTRY
CN   Glycinamide, glycylglycyl-L-phenylalanyl-N-[(1S,9S)-9-ethyl-5-fluoro-
     2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-
     benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]-,
     mono(trifluoroacetate) (salt) (9CI)  (CA INDEX NAME)
SQL  4

SEQ      1 GGFG
            ====
HITS AT:    1-4

SEQ      1 GGFG
            ====
HITS AT:    1-4

SEQ      1 GGFG
            ====
HITS AT:    1-4

REFERENCE   1:  130:316621

L8   ANSWER 15 OF 40  REGISTRY  COPYRIGHT 2002 ACS
RN   223537-08-4  REGISTRY
CN   Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-
     phenylalanyl-N-[(1S,9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-
     hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indoli
     zino[1,2-b]quinolin-1-yl]- (9CI)  (CA INDEX NAME)
```

CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:74660

REFERENCE 2: 130:316621

L8 ANSWER 16 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **219657-42-8** REGISTRY
CN 1-7-Sperm-activating peptide f (Tripneustes gratilla egg jelly coat), N-[N-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]glycyl]-, (4-carboxyphenyl)methyl ester (9CI) (CA INDEX NAME)
SQL **8**

SEQ 1 GGFGLGGG
====
HITS AT: 1-4

REFERENCE 1: 130:106811

L8 ANSWER 17 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **200427-88-9** REGISTRY
CN Glycine, glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:139833

REFERENCE 2: 136:123681

REFERENCE 3: 135:185307

REFERENCE 4: 132:326152

REFERENCE 5: 128:66510

REFERENCE 6: 128:66509

L8 ANSWER 18 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **193097-95-9** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4-ethyl-3,4,12,13-tetrahydro-4-hydroxy-3,13-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, compd. with dextran carboxymethyl ether sodium salt (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dextran, carboxymethyl ether, sodium salt, compd. with glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4-ethyl-3,4,12,13-tetrahydro-4-hydroxy-3,13-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]glycinamide (9CI)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 134:256691

REFERENCE 2: 127:135979

L8 ANSWER 19 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-34-7** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[(9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 20 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-33-6** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 134:256691

REFERENCE 2: 130:287052

REFERENCE 3: 127:135979

L8 ANSWER 21 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-32-5** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4-ethyl-3,4,12,14-tetrahydro-4-hydroxy-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 134:256691

REFERENCE 2: 130:287052

REFERENCE 3: 127:135979

L8 ANSWER 22 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-25-6** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 23 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-24-5** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 24 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-23-4** REGISTRY
CN L-Phenylalaninamide, glycylglycyl-N-[2-[4-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]-1-piperazinyl]-2-oxoethyl]-, monohydrochloride (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 25 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-22-3** REGISTRY
CN L-Phenylalaninamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-N-[2-[4-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 26 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-20-1** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(9S)-9-ethyl-2,3,9,10,13,15-hexahydro-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]propyl]-, monohydrochloride (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 27 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192991-18-7** REGISTRY
CN Glycinamide, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl-N-[3-[[(9S)-9-ethyl-2,3,9,10,13,15-hexahydro-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]propyl]- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

REFERENCE 2: 127:135979

L8 ANSWER 28 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192990-96-8** REGISTRY

CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[(9S)-9-ethyl-5-fluoro-2,3,9,10,13,15-hexahydro-9-hydroxy-4-methyl-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-1-yl]- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

L8 ANSWER 29 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192990-95-7** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(4S)-4-ethyl-3,4,12,13-tetrahydro-4-hydroxy-3,13-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl]oxy]propyl]- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

L8 ANSWER 30 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192990-94-6** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

L8 ANSWER 31 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192990-93-5** REGISTRY
CN L-Phenylalaninamide, glycylglycyl-N-[2-[4-[[(8S)-8-ethyl-2,3,8,9,12,14-hexahydro-8-hydroxy-9,12-dioxo-11H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-15-yl]methyl]-1-piperazinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

L8 ANSWER 32 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **192990-91-3** REGISTRY
CN Glycinamide, glycylglycyl-L-phenylalanyl-N-[3-[[(9S)-9-ethyl-2,3,9,10,13,15-hexahydro-9-hydroxy-10,13-dioxo-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl]oxy]propyl]- (9CI) (CA INDEX NAME)
CI COM
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 130:287052

L8 ANSWER 33 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **187794-49-6** REGISTRY
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]glycylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 136:74660

REFERENCE 2: 134:256691

REFERENCE 3: 132:15631

REFERENCE 4: 130:316621

REFERENCE 5: 130:287052

REFERENCE 6: 127:135979

REFERENCE 7: 126:199707

L8 ANSWER 34 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **177261-43-7** REGISTRY
CN Glycine, N-[N-[N-[N-(N2-L-valyl-L-arginyl)glycyl]glycyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)
SQL **6**

SEQ 1 VRGGFG
====
HITS AT: 3-6

REFERENCE 1: 125:2993

L8 ANSWER 35 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **169692-79-9** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-hydroxy-, ester with N-[N-[N-(N-L-tyrosylglycyl)glycyl]-L-phenylalanyl]glycine (9CI) (CA INDEX NAME)
CI PMS
SQL **5**

SEQ 1 YGGFG
====
HITS AT: 2-5

REFERENCE 1: 125:34037

REFERENCE 2: 123:286659

L8 ANSWER 36 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **161254-06-4** REGISTRY
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[(glycylglycyl-L-phenylalanylglycyl)amino]-.alpha.-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S,10S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5,12-Naphthacenedione, 7,8,9,10-tetrahydro-6,8,11-trihydroxy-8-(hydroxyacetyl)-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[N-(N-glycylglycyl)-L-phenylalanyl]glycyl]amino]-.alpha.-L-lyxo-hexopyranosyl]oxy]-, monohydrochloride, (8S-cis)-
SQL **4**

SEQ 1 GGFG
====
HITS AT: 1-4

REFERENCE 1: 133:155250

REFERENCE 2: 128:30115

REFERENCE 3: 124:176877

REFERENCE 4: 122:299074

L8 ANSWER 37 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **153012-44-3** REGISTRY
CN .beta.-Alanine, N-[N-[N-[N-(N-L-tyrosylglycyl)glycyl]-L-phenylalanyl]glycyl]- (9CI) (CA INDEX NAME)
SQL **6**

SEQ 1 YGGFGX
====
HITS AT: 2-5

REFERENCE 1: 120:123965

L8 ANSWER 38 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **143740-83-4** REGISTRY
CN L-Phenylalaninamide, L-tyrosylglycylglycyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)
SQL **6**

SEQ 1 YGGFGF
====
HITS AT: 2-5

REFERENCE 1: 117:167122

L8 ANSWER 39 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **87742-82-3** REGISTRY
CN Glycine, glycylglycyl-L-phenylalanylglycyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glycine, N-[N-[N-(N-glycylglycyl)-L-phenylalanyl]glycyl]-
OTHER NAMES:
CN 10: PN: US6271197 SEQID: 20 unclaimed sequence
CN 18: PN: US6277564 SEQID: 18 unclaimed sequence
SQL **5**

SEQ 1 GGFGG
====
HITS AT: 1-4

REFERENCE 1: 135:191315

REFERENCE 2: 135:162483

REFERENCE 3: 100:82203

L8 ANSWER 40 OF 40 REGISTRY COPYRIGHT 2002 ACS
RN **61064-76-4** REGISTRY
CN Glycine, N-[N-[N-(N-L-tyrosylglycyl)glycyl]-L-phenylalanyl]- (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN 5-Gly-enkephalin
CI COM
SQL **5**

Q 1 YGGFG
====
HITS AT: 2-5

REFERENCE 1: 113:78941

REFERENCE 2: 94:96684

REFERENCE 3: 89:17351

REFERENCE 4: 88:16289

REFERENCE 5: 85:186907

FILE 'HOME' ENTERED AT 15:18:00 ON 15 JUL 2002